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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,466	07/19/2001	Andrei W. Konradi	002010-676	1745

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EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT PAPER NUMBER

1624

DATE MAILED: 07/09/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/910,466

Applicant(s)

KONRADI ET AL.

Examiner

Tamthom N. Truong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 17, and 19-23 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 29 is/are allowed.
- 6) ☒ Claim(s) -16, 18, and 24-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4,8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-16, 18, and 24-28) in Paper No. 10 is acknowledged. The traversal is on the ground(s) that there is no burden of searching. This is not found persuasive because of the following reasons:

- a. Although compounds of formula I are derivatives of alanine, a search for 'alanine derivatives' will yield an inexhaustive number of hits. Besides, "alanine" does not contribute to the patentability of the compounds. It is the **combination** of rings A, HetAr, and alanine chain that sets apart compounds in groups I-V. Also, when HetAr is an indolyl-methyl, then the side chain becomes a "tryptophan", and not "alanine" anymore. So, searching "alanine derivatives" alone would miss relevant references. Thus, the burden of searching exists when the combination of rings A, HetAr, and the side chain.
- b. Note, groups I-V could have been further restricted at HetAr since said variable practically embraces the entire heteroaryl class.
- c. Group VI is drawn to method of treatment using compounds in groups I-V. However, a search for the compounds does not necessarily yield the same method of treatment (as evident by the references cited in the art rejections below). It is recognized that claim 1 recites the functional language of "binding affinity to VLA-4", but said limitation does not have patentable weight since the specification generalizes that the claimed compounds have such a binding affinity. Thus, a search for group VI requires a scope beyond that of the compound and composition claims.

The requirement is still deemed proper and is therefore made FINAL.

Note, claim 29 has been inadvertently left out from Group I. Thus, the elected group now includes claims 1-16, 18, and 24-29 remain pending while claims 17, and 19-23 are withdrawn from consideration as being drawn to non-elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-16, 18, and 24-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. In claim 1, the functional limitation of "binding affinity to VLA-4..." does not appear to further limit the scope of formula (I). It is unclear which compounds of formula (I) are intended, if not all.

b. Claims 11, 13-16, and 25-28 lack antecedent basis because they include compounds and pharmaceutical compositions of formula IIa which have been deleted from the amended claim 1. Note, claim 1 no longer recites A having substituents of "-NR(SO₂)....", or "-N[S(O)₂R']₂". In essence, compounds of formula IIa have been excluded.

- c. Claims 2-10, 18, and 24 are rejected as being dependent on claim 1 and carrying over its limitations.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2, 8, 10, 18, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by the following references:

a. **Ulane et. al.** (CA 76:25548s): The compound of formula I with X as Br and R as DL-tryptophanyl reads on a compound of formula (I) {in claims 1, 2, 8, 10, 18, and 24} with the following substituents:

- i. A represents a pyrimidinyl ring substituted with halogens;
- ii. HetAr is a nitrogen containing heteroaryl group (i.e., 3-indolyl); m = 1;
- iii. X is hydroxyl.

b. **Ueda et. al.** (J. Med. Chem., (1963), 6(6), pp. 697-701): Compounds IVd and VIII (on page 698 or 700) read on compounds of formula (I) {in claims 1, 2, 10, 18, and 24} with the following substituents:

- i. A represents a pyrimidinyl ring substituted with an oxo or thio;

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- ii. HetAr is a nitrogen containing heteroaryl group (specifically, 3-indolyl);
m = 1.
- iii. X is hydroxyl;

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 2, 10, 18, and 24 are rejected under 35 U.S.C. 102(e) as being inherently anticipated by **Gonzalez et. al.** (US 2002/0169101): On column 43 of US'101, Example 20 inherently discloses an intermediate (i.e., "the acid from step 1") that reads on a compound of formula (I) with the following substituents:

- i. A represents a pyrimidinyl ring;
- ii. HetAr is a nitrogen containing heteroaryl group (specifically, 3-indolyl);
m = 1.
- iii. X is hydroxyl; R¹ represents an alkyl group.

Note, although claim 1 recites the limitation of a “binding affinity to VLA-4”, the instant specification urges that all compounds of formula (I) have such a “binding affinity to VLA-4”, see the following excerpt from page 108:

When tested in this assay, each of the compound prepared in the above examples has or is expected [emphasis added] to have an IC_{50} of 15 μM or less (or is expected to be active in vivo).

Since the instant specification does not indicate which compounds not having a “binding affinity to VLA-4”, it is expected that any compound of formula (I) would have such a binding affinity. Therefore, the compounds of the cited references would be expected to have the same “binding affinity to VLA-4” due to structural similarity.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1, 2, 10, 18, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Gonzalez et. al.** (US 2002/0169101). As discussed in the above 102(e) rejection, Example 20 suggests an acid that is embraced by the instant formula (I). Although the reference does not cite the name of said acid, one of the ordinary skill in the art can deduce such an acid from the

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process in Example 17 (page 42). Thus, it is obvious that the acid in Example 20 should be '2-(pyrimidin-5-ylamino)-3-(1H-indol-3-yl-methyl)-2-methylpropionic acid'. The disclosed acid is used as an intermediate. However, one skilled in the art would have been motivated to make such an acid since its preparation had been described. Furthermore, one could always use said acid as an intermediate. See *In re Dillon* 16 USPQ 2d. 1897, 1923 regarding a prima facie case of obviousness of structurally similar compounds disclosed by a prior art "regardless of the properties disclosed in the inventor's application".

Again, the limitation of "binding affinity to VLA-4" in claim 1 does not impart patentability since the instant specification does not cite compounds without "binding affinity to VLA-4".

Claim Objections

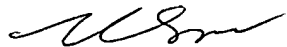
6. Claim 29 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior arts of record do not teach or suggest compounds recited in claim 29.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (9:30-5:00) & every Saturday morning (starting from 4-7-03).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Tamthom N. Truong
Examiner
Art Unit 1624

July 8, 2003